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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/089,501	04/22/2002	Hiroyuki Saito	053466-0325	9449

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EXAMINER	
BURKHART, MICHAEL D	
ART UNIT	**PAPER NUMBER**
1633	

DATE MAILED: 04/18/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/089,501	SAITO ET AL.	
	Examiner	Art Unit	
	Michael D. Burkhart	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *45-53* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/20/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 3/20/2006 has been entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 45-53 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a New Matter rejection.**

Amended claim 45 (from which all other claims depend) recites a method for "suppressing the growth of blood vessel tissues in a patient in need thereof." Thus, the claimed subject matter has been broadened to include treatment of angiogenesis and neovascularization, in addition to stenosis and restenosis. The response indicates support for the amendment may be found on pages 40-41 of the specification. These pages recite an Example wherein pre-treatment

with the i-b2 monoclonal antibody suppressed growth of the blood vessel lumen (i.e. intima) in response to physical injury. While this is a single example of treatment of restenosis, it does not provide support for angiogenesis or neovascularization. Therefore, there appears to be no support for the broadened scope of the claims. Thus, the amended claims include impermissible New Matter.

Furthermore, applicants claim methods for "suppressing the growth of blood vessel tissues in a patient in need thereof" by administration of an antibody to human tissue factor (human TF). Applicants disclose a single example and antibody, i-b2, used in a method of suppressing the growth of the vascular lumen in response to injury. The claims read on a broad genus of methods and human TF antibodies to suppress the growth of blood vessel tissues.

The written description requirement for a genus may be satisfied by sufficient description of a representative number of species by actual reduction to practice or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function, or by a combination of such identifying characteristics, sufficient to show that applicant was in possession of the claimed invention. In the instant case, applicants only disclose a single antibody, i-b2, capable of suppressing the growth of lumenal blood vessel tissues. Neither applicants nor the prior art disclose other human TF antibodies capable of suppressing the growth of blood vessel lumen as claimed. The remainder of the instant disclosure is directed to the inhibition of blood clot formation (e.g. thrombosis) rather than the inhibition of lumenal blood vessel tissue. Therefore, applicants claim the human TF antibodies for suppression of

blood vessel tissues by function only, without a correlation between structure and function. The diversity of the possible human TF antibodies involved coupled with the lack of disclosure regarding human TF antibodies other than i-b2 that function as claimed, would require the skilled artisan to conclude that the single example presented by the applicants is not sufficient to describe the claimed genus.

Claims 45-53 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using human TF antibodies to suppress restenosis, does not reasonably provide enablement for using human TF antibodies to suppress any other types of blood vessel growth, e.g. angiogenesis or neovascularization. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. The claims broadly recite a method of inhibiting blood vessel growth by administration of human TF antibodies. Types of blood vessel growth include stenosis, restenosis, angiogenesis, and neovascularization. The instant specification discloses the use of one human TF monoclonal antibody (i-b2) to suppress restenosis, and does not mention the use of human TF antibodies to suppress blood vessel growth related to angiogenesis or neovascularization.

The test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosures in the application coupled with information known in the art without undue experimentation (*United States v. Telectronics,* Inc. 8 USPQD2d 1217 (Fed. Cir. 1988)). Whether undue experimentation is required is a conclusion reached by weighing several

factors. These factors were outlined in *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Inter. 1986) and again in *In re Wands*, 8 USPQQ2d 1400 (Fed. Cir. 1988) and include the following:

Unpredictability of the art. The art concerning inhibition of blood vessel tissue growth by administration of human TF antibodies is unpredictable. There is no mention of the administration of such antibodies to patients in need of angiogenesis inhibition (e.g. cancer patients) in the prior art, or in applicants' disclosure. In a review of angiogenesis inhibitors published in 2004 (five years after applicants filing date), Eskens (British J. Cancer, 2004) teaches antibodies specific for VEGF or VEGFR as angiogenesis inhibitors, but there is no mention of human TF antibodies as inhibitors of angiogenesis. Thus, the effects of administering human TF antibodies to a patient in need of suppression of angiogenesis or neovascularization are unknown, and therefore unpredictable.

State of the art. The state of the art regarding the inhibition of blood vessel tissue growth by administration of human TF antibodies is poorly developed. The development of efficacious human TF antibodies would have to be done empirically, along with the development of the appropriate methods (e.g. dosage, delivery).

Number of working examples. Applicants have provided a working example of inhibiting restenosis with a human TF antibody. Applicants have provided no working examples of human TF antibodies that suppress any other types of blood vessel tissue growth (e.g. angiogenesis), nor methods of administering such antibodies.

Amount of guidance. Other than restenosis, applicants provide no direction or guidance for the claimed methods of inhibiting other types of blood vessel tissue growth by administration of human TF antibodies. The specification requires the skilled artisan to practice trial and error

experimentation with different human TF antibodies, dosage limitations, and administration methods to determine which (if any) will be efficacious as claimed.

Scope of the invention. The claims are broad in nature and read on the administration of any human TF antibody to a patient in need of suppression of blood vessel tissue growth, regardless of the type of blood vessel tissue involved (e.g. the claims read on a method to treat all cancers).

Nature of the invention. The invention involves the unpredictable art of treating blood vessel tissue growth with human TF antibodies.

Level of skill in the art. While the level of skill in the art of treating hypercoagulation-related diseases with human TF antibodies is high, the level of skill in the art of suppressing blood vessel tissue growth with such antibodies is low. The unpredictability of the art, lack of guidance, broad scope of the claims and poorly developed state of the art would require that undue and excessive experimentation would have to be conducted by the skilled artisan in order to practice the claimed invention.

Given the above analysis of the factors which the courts have determined are critical in determining whether a claimed invention is enabled, it must be considered that undue and excessive experimentation would have to be conducted by the skilled artisan in order to practice the claimed invention.

Claim Objections

Claim 51 recites antibodies with a defined amino acid sequence, i.e. the b-b, i-b, or i-b2 antibody versions as found in Tables 1-3 on pages 23-25 of the specification, which are

associated with SEQ ID NOs. Thus, the SEQ ID NOs are essential to the claimed antibodies and should be recited in the claims.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael D. Burkhart whose telephone number is (571) 272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael D. Burkhart
Examiner
Art Unit 1633

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER